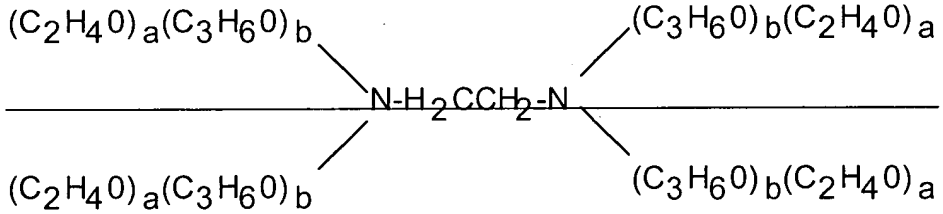
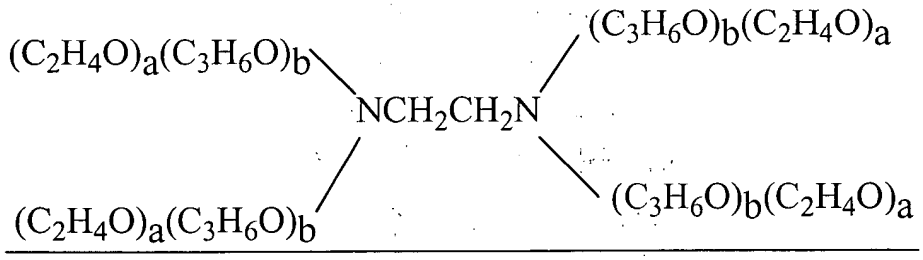
Amendments to the Specification

In accordance with revised 37 C.F.R. § 1.121, please amend the specification as follows, with deletions shown by strikethrough and additions shown by underlining:

Please amend the paragraph beginning on page 8, line 31 and ending on page 9, line 26 as follows:

In another aspect, the present invention comprises a therapeutic delivery composition effective for treating a disease state"," comprising an administerable admixture of an effective amount of a therapeutic compound capable of altering nucleic acid sequence function and an effective amount of a biologically-active copolymer"," comprising a copolymer of polyoxyethylene (POE)"," which is hydrophilic"," and polyoxypropylene (POP)"," which is hydrophobic. The block copolymer is built on a tetrafunctional ethylenediamine initiator. In the preferred embodiment of the biologically-active copolymers of the present invention, the block copolymers that comprise the biologically-active copolymers of the present invention have the following general formulas:





POE **POP** **POP** **POE**

wherein:

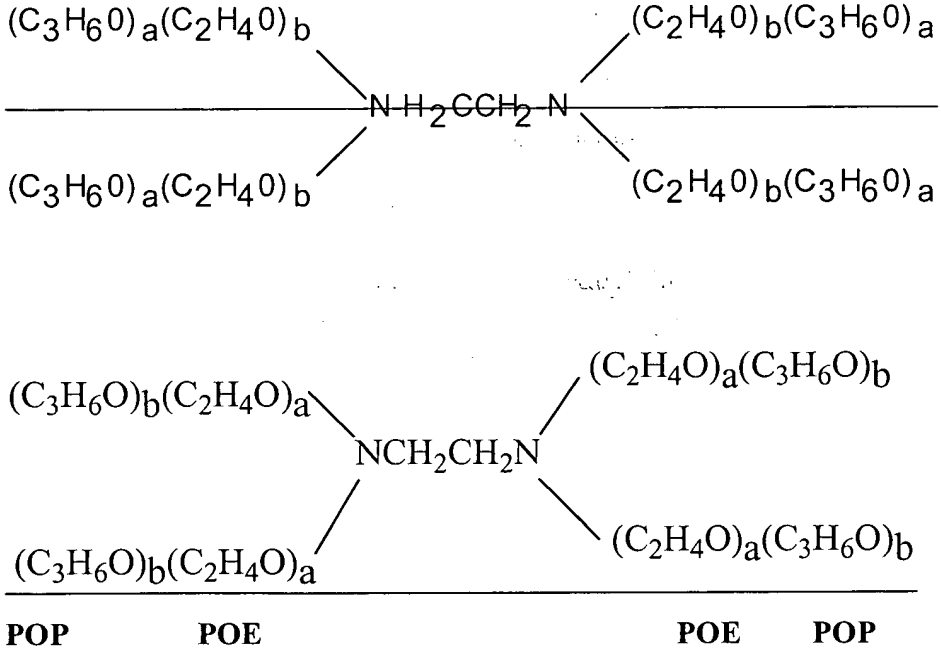
the mean aggregate molecular weight of the hydrophobe portion of the octablock copolymer consisting of polyoxypropylene $(C_3H_6O)_b$ (POP) is between approximately 5000 and 7000 ~~daltons~~ Daltons;

a is a number such that the hydrophile portion represented by polyoxyethylene $(C_2H_4O)_a$ (POE) constitutes between approximately 10% to 40% of the total molecular weight of the ~~compound~~ octablock copolymer; and

b is a number such that the polyoxypropylene $(C_3H_6O)_b$ (POP) portion of the total molecular weight of the octablock copolymer constitutes between approximately 60% and 90% of the ~~compound~~ copolymer.

Please amend the paragraph beginning on page 9, line 27 and ending on page 10, line 20 as follows:

In another aspect of the present invention, the biologically-active copolymer comprises a polymer of hydrophilic polyoxyethylene (POE) built on an ethylene diamine initiator. Polymers of hydrophobic polyoxypropylene (POP) are then added to the blocks of hydrophilic polyoxyethylene (POE). This results in an octablock copolymer with the general formula:



wherein:

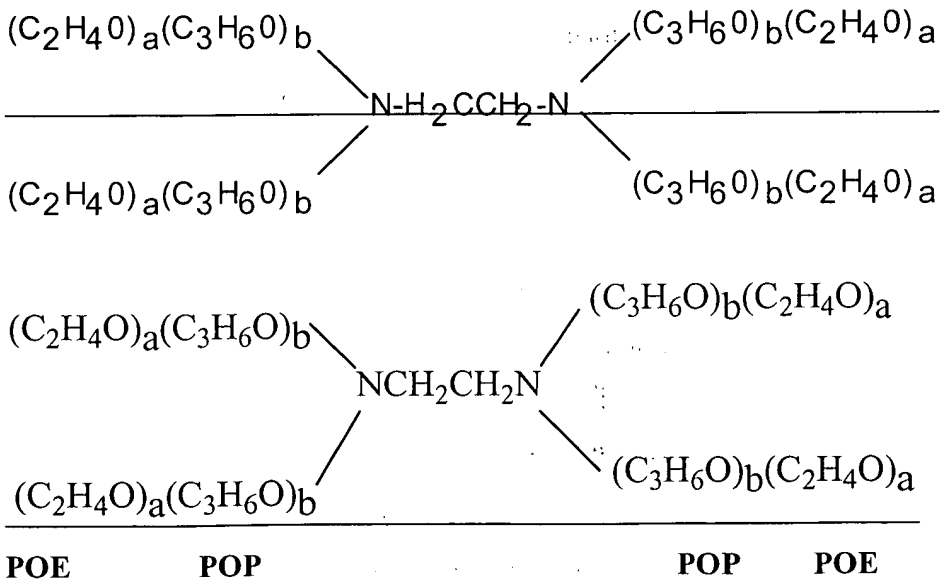
a is a number such that the hydrophile portion represented by polyoxyethylene $(C_2H_4O)_a$ (POE) constitutes between approximately 10% to 40% of the total molecular weight of the ~~compound~~ octablock copolymer;

the mean aggregate molecular weight of the hydrophobe portion of the octablock copolymer consisting of polyoxypropylene $(C_3H_6O)_b$ (POP) is between approximately 5000 and 7000 ~~daltons~~ Daltons; and

b is a number such that the polyoxypropylene $(C_3H_6O)_b$ (POP) portion of the total molecular weight of the octablock copolymer constitutes between approximately 60% and 90% of the ~~compound~~ copolymer.

Please amend the paragraph beginning on page 26, line 11 and ending on page 27, line 6 as follows:

In one aspect of the biologically active POE/POP copolymers of the present invention, the block copolymer comprises a polymer of hydrophobic polyoxypropylene (POP) built on an ethylenediamine initiator. Polymers of hydrophilic polyoxyethylene (POE) are then built on the ~~block~~ blocks of hydrophobic polypropylene (POP). This results in an octablock copolymer with the following general formula:



wherein:

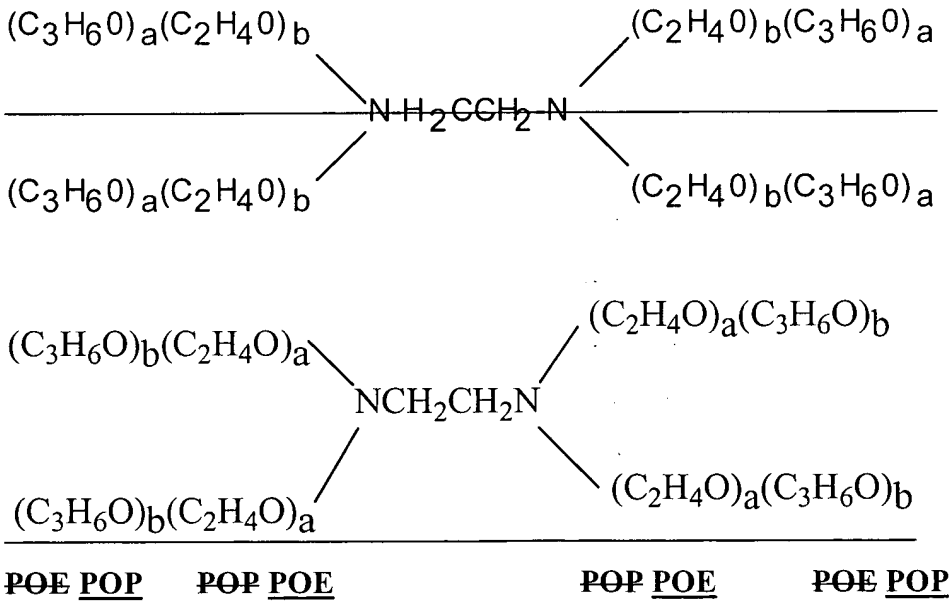
the mean aggregate molecular weight of the hydrophobe portion of the octablock copolymer consisting of polyoxypropylene $(C_3H_6O)_b$ (POP) is between approximately 5000 and 7000 ~~daltons~~ Daltons;

a is a number such that the hydrophile portion represented by polyoxyethylene $(C_2H_4O)_a$ (POE) constitutes between approximately 10% to 40% of the total molecular weight of the ~~compound~~ octablock copolymer; and

b is a number such that the polyoxypropylene $(C_3H_6O)_b$ (POP) portion of the total molecular weight of the octablock copolymer constitutes between approximately 60% and 90% of the ~~compound~~ copolymer.

Please amend the paragraph beginning on page 27, line 7 and ending on page 27, line 31 as follows:

In another aspect of the present invention, the POE/POP block copolymer comprises a polymer of hydrophilic polyoxyethylene (POE) built on an ethylene diamine initiator. Polymers of hydrophobic polyoxypropylene (POP) are then built on the ~~block~~ blocks of hydrophilic ~~polyethylene~~ polyoxyethylene (POE). This results in an octablock copolymer with the general formula:



wherein:

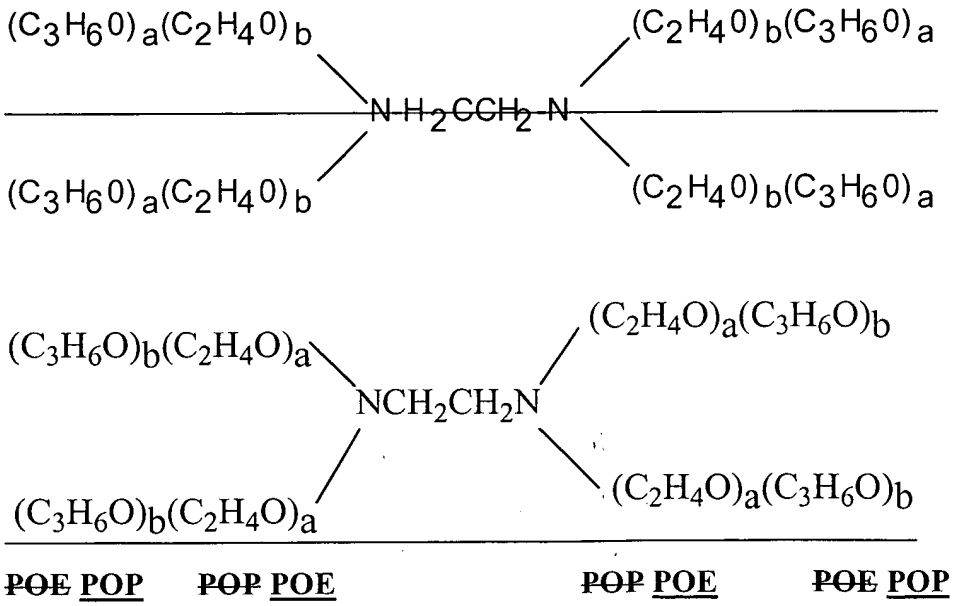
~~The~~ the molecular weight of the hydrophobe portion of the octablock copolymer consisting of polyoxypropylene $(C_3H_6O)_b$ (POP) is between approximately 5000 and 7000 ~~daltons~~ Daltons;

a is a number such that the hydrophile portion represented by polyoxyethylene $(C_2H_4O)_a$ (POE) constitutes between approximately 10% and 40% of the total molecular weight of the ~~compound~~ octablock copolymer; and

b is a number such that the polyoxypropylene $(C_3H_6O)_b$ (POP) portion of the octablock copolymer constitutes between approximately 60% and 90% of the ~~compound~~ copolymer.

Please amend the paragraph beginning on page 28, line 23 and ending on page 29, line 10 as follows:

A preferred biologically active copolymer is the octablock copolymer T110R1 (BASF Corporation, Parsippany, NJ) which corresponds to the following formula:



wherein:

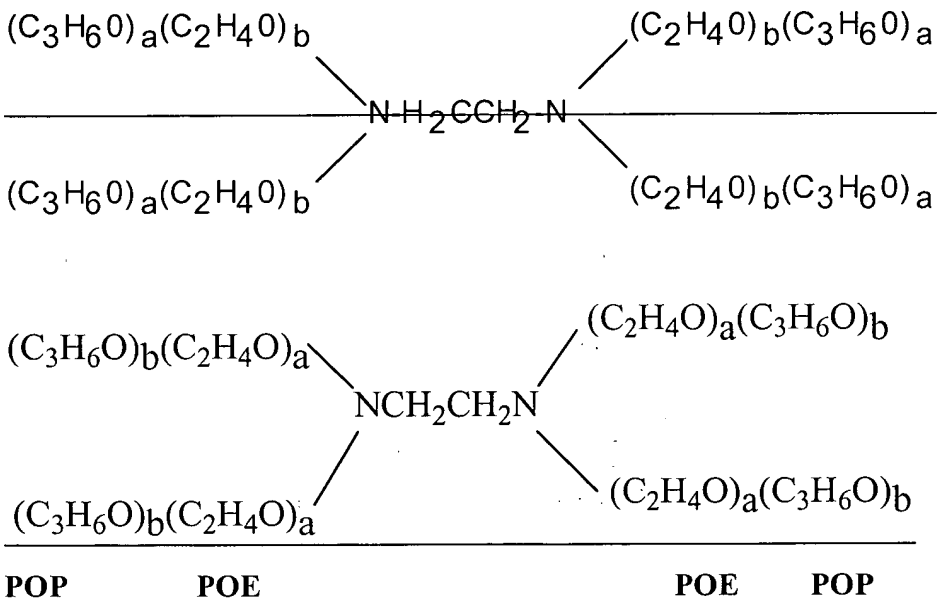
~~The~~ the mean molecular weight of the hydrophobe portion of the octablock copolymer represented by polyoxypropylene $(C_3H_6O)_b$ (POP) is between approximately 5,220 ~~daltons~~ Daltons;

a is a number such that the hydrophile portion represented by polyoxyethylene $(C_2H_4O)_a$ (POE) constitutes between approximately 10% of the ~~compound~~ octablock copolymer by weight; and

b is a number such that the polyoxypropylene $(C_3H_6O)_b$ (POP) portion of the octablock copolymer constitutes approximately 90% of the ~~compound~~ copolymer by weight.

Please amend the paragraph beginning on page 29, line 11 and ending on page 29, line 29 as follows:

A preferred biologically active ~~copolymers~~ copolymer is the octablock copolymer T130R2 (BASF Corporation, Parsippany, NJ) which corresponds to the following formula:



wherein:

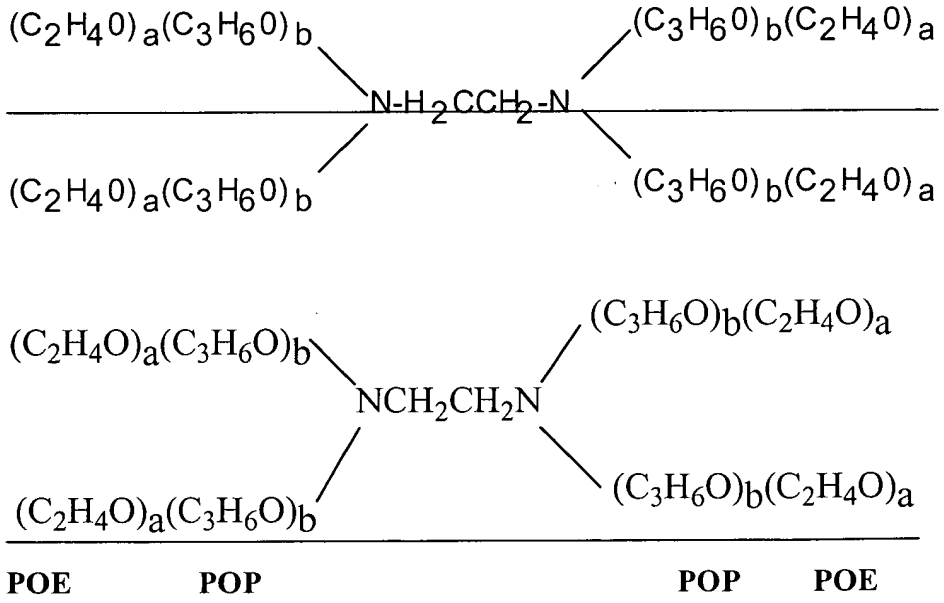
~~The~~ the mean molecular weight of the hydrophobe portion of the octablock copolymer represented by polyoxypropylene $(C_3H_6O)_b$ (POP) is between approximately 5750 ~~daltons~~ Daltons;

a is a number such that the hydrophile portion represented by polyoxyethylene $(C_2H_4O)_a$ (POE) constitutes approximately 20% of the ~~compound~~ octablock copolymer by weight; and

b is a number such that the polyoxypropylene $(C_3H_6O)_b$ (POP) portion of the octablock copolymer constitutes approximately 80% of the ~~compound~~ copolymer by weight.

Please amend the paragraph beginning on page 29, line 30 and ending on page 30, line 19 as follows:

Another preferred embodiment of the biologically active copolymers of the present invention is the ~~compound~~ copolymer designated T1501 (BASF Corporation, Parsippany, NJ) which corresponds to the following formula:



wherein:

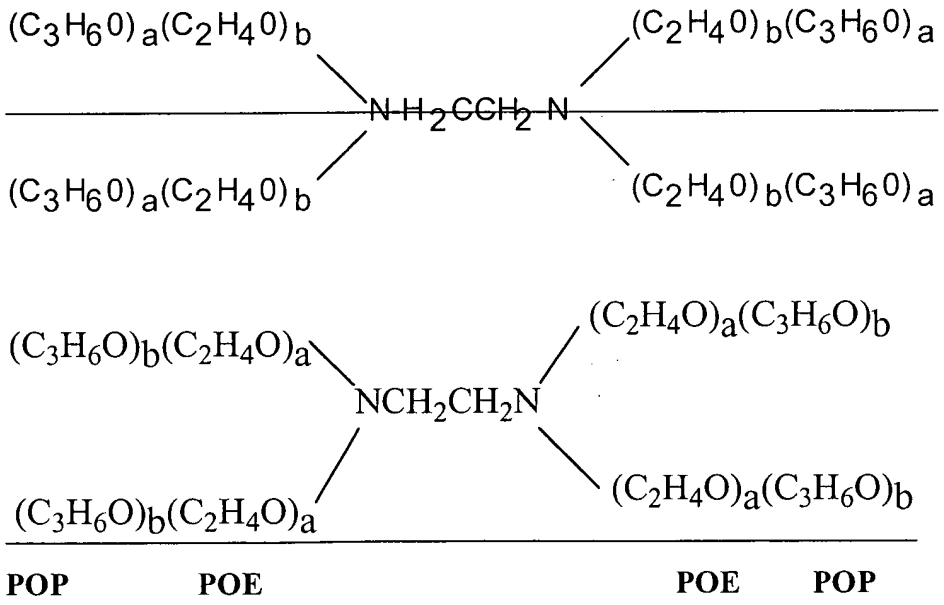
the mean molecular weight of the hydrophobe portion of the octablock copolymer represented by polyoxypropylene $(C_3H_6O)_b$ (POP) is between approximately 6750 ~~daltons~~ Daltons;

a is a number such that the hydrophile portion represented by polyoxyethylene $(C_2H_4O)_a$ (POE) constitutes between approximately 10% of the ~~compound~~ octablock copolymer by weight; and

b is a number such that the polyoxypropylene $(C_3H_6O)_b$ (POP) portion of the octablock copolymer constitutes approximately 90% of the ~~compound~~ copolymer by weight.

Please amend the paragraph beginning on page 30, line 20 and ending on page 31, line 11 as follows:

The most preferred embodiment of the biologically active copolymers of the present invention is the octablock copolymer T150R1 (BASF Corporation, Parsippany, NJ) which corresponds to the following formula:



wherein:

~~The~~ the mean molecular weight of the hydrophobe portion of the octablock copolymer represented by polyoxypropylene $(C_3H_6O)_b$ (POP) is between approximately 6750 ~~daltons~~ Daltons;

a is a number such that the hydrophile portion represented by polyoxyethylene $(C_2H_4O)_a$ (POE) constitutes approximately 10% of the ~~compound~~ octablock copolymer by weight; and

b is a number such that the polyoxypropylene $(C_3H_6O)_b$ (POP) portion of the octablock copolymer constitutes approximately 90% of the ~~compound~~ copolymer by weight.

Please delete the paragraph beginning 'The present invention', on page 31, line 12 and ending on page 31, line 19.

Please amend the paragraph beginning on page 34, line 19 and ending on page 34, line 23 as follows:

For example, an antisense oligonucleotide sequence, such as one of those disclosed by ~~Matsukara~~ Matsukura, M. et al., *Proc. Natl. Acad. Sci.* USA 84:7706-7710 (1987), which is expressly incorporated herein in its entirety by reference, is combined with the copolymer to form a micelle composition.

Please amend the paragraph beginning on page 34, line 24 and ending on page 35, line 6 as follows:

Briefly, phosphorothioate or methylphosphonate derivatives of a sequence complimentary to regions of the *art/trs* genes of HIV having the sequence 5'-TCGTCGCTGTCTCG-3' (SEQ ID NO:1) are prepared according to the method of Matsukura et al. Three hundred ~~300~~ milligrams (300 mg) of CRL-8131 is added to 10 ml of 0.9% NaCl, and the mixture is solubilized by storage at temperatures of 2-4°C, until a clear solution is formed. The desired antisense oligonucleotide subsequently is mixed with the copolymer solution to provide a concentration effective in inhibiting viral activity when administered to a patient infected with the HIV virus. Generally the effective amount of antisense compound

will be such that the final concentration in the blood is in the range of 1 μM to 100 μM, although other effective amounts of antisense compounds outside this range may be found for specific antisense compounds. One skilled in the art can readily test the relative effectiveness of any particular antisense oligonucleotide according to the *in vivo* test of Matsukura et al.